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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,653	01/22/2004	Leonard Schlessinger	8223.002.CPUS02	8542

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EXAMINER	
SIMS, JASON M	

ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
09/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/763,653	SCHLESSINGER ET AL.	
	Examiner	Art Unit	
	JASON M. SIMS	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,31-40,52 and 61-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 31-40, 52, and 61-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 6/10/2008, have been fully considered. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-10, 31-40, 52, and 61-75 are the current claims hereby under examination.

Claim Rejections - 35 USC § 112-Partly withdrawn

Response to Arguments:

Applicant's arguments, filed 12/20/2007, with respect to rejections of Claims 4, 34, and 67 and all claims dependent therefrom for comprising xi..sub.3 and xi..sub.2 in the equation whereas the claim language addresses xi..sub.1 and xi..sub.3, which causes said claims to be vague and indefinite have been fully considered and are persuasive because of applicant's amendments and arguments. Therefore the rejections have been withdrawn.

Applicant's arguments, filed 12/20/2007, with respect to rejections of Claims 6, 36, and 69 and all claims dependent therefrom comprise xi..sub.3, which is vague and indefinite as to whether this is the same xi..sub.3 as in claims 4, 34, and 67 have been fully considered and are persuasive because of applicant's amendments and arguments. Therefore the rejections have been withdrawn.

Applicant's arguments, filed 12/20/2007, with respect to rejections of Claims 10, 40, and 73 and all claims dependent therefrom comprise the variable I or 1, which is vague and indefinite have been fully considered and are persuasive because of

applicant's amendments and arguments. Therefore the rejections have been withdrawn.

Applicant's arguments, filed 12/20/2007, with respect to rejections of Claims 5, 35, and 68 comprising the vague and indefinite variables a, b, c, and d to calculate RBMI have been fully considered and are persuasive because of applicant's amendments and arguments. Therefore the rejections have been withdrawn.

Applicant's arguments, filed 12/20/2007, with respect to rejections of Claims 4, 34, and 67 and all claims dependent therefrom comprising the wording "randomizing the virtual patient within the population," which is vague and indefinite have been fully considered and are persuasive because of applicant's amendments and arguments. Therefore the rejections have been withdrawn.

Claim Rejections - 35 USC § 112-Partly Maintained

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 7, 10, 33, 40, 66, 70, and 73 and all claims dependent therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 7, 10, 33, 40, 66, 70, and 73 and all claims dependent therefrom comprise the term DF_2, which is defined in claim 4 as representing an incidence of disease. However the specification defines the instant term as representing "causes of

diabetes." Therefore, it is unclear as to what exactly one is to plug into this equation and it is vague and indefinite as how this term represents incidence of diabetes. Clarification via clearer claim wording is required.

Response to Arguments:

Applicant's arguments filed 6/10/2008 have been fully considered but they are not persuasive.

Applicant argues that the provided definition "DF2 is a type 2 diabetes feature that represents an incidence of type 2 diabetes for the virtual patient" satisfies any vague and indefiniteness of the variable.

Applicant's arguments are not persuasive because the wording "diabetes feature" does not further clarify what it is exactly that the variable DF2 represents. Furthermore, turning to the instant specification at paragraph [0160] states the DF2 variable as representing "the causes of diabetes." Moreover, at paragraph [0193] applicant states "more specifically, the diabetes features do not determine the progression of a patient to a "state" called "diabetes". Rather, the features determine the progression of the underlying biological phenomena that determine a person's glucose level at any time." In addition, at paragraph [0226] applicant states that the variable DF2 "incorporates the degree of control of the disease over time." Therefore it is unclear as to what diabetes feature the DF2 variable represents or if it represents the causes of diabetes and whether that is considered different from representing an incidence of diabetes for a virtual patient. Clarification via clearer claim wording is required.

Claims 3, 8, 9, 33, 38, 39, 40, 66, 71, 72, and 75 and all claims dependent therefrom all comprise the variables either a and b or a, b, c, and d and define them as being set to fit data for a population, which has been deemed as vague and indefinite. It is unclear as to which population these values are being set to, such as a virtual population or real population and how they are being fit. It is unclear from the specification as to how the instant variables or which method is being used for said fitting of said variables. Clarification via clearer claim wording is required.

Response to Arguments:

Applicant's arguments filed 6/10/2008 have been fully considered but they are not persuasive.

Applicant argues that defining said parameters as set to fit data for a population that is represented by the virtual patient overcomes the vague and indefiniteness of said variables. Furthermore, applicant argues that a population may be defined or characterized by "Race/ethnicity and sex."

Applicant's arguments are not persuasive as it is unclear as to how these variables are being fit to a population that is represented by a virtual patient. Furthermore, in the instant specification at paragraph [0163], applicant states that "race/ethnicity and sex are included through the values of the parameters a, b, c, d, e, and f." It is unclear as to how they are included through the parameters. It also appears that race/ethnicity and sex are interchangeable with respect to any of the parameters a, b, c, d, e, or f. Clarification via clearer claim wording is required.

Claim Rejections - 35 USC § 103-Maintained

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-2, 31-32, 52, 61, 63, 65, and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over van Holde (1996).

The claims are drawn to a method for estimating a virtual patient's fasting plasma glucose level, comprising: determining the virtual patient's basal hepatic production; determining the virtual patient's insulin level; calculating the virtual patient's fasting blood glucose at time t by solving an equation where the virtual patient's fasting blood glucose level at time t is equal to the basal hepatic production divided by the insulin level and efficiency of insulin use.

Van Holde (1996) at page 824-825 teaches the role of insulin in the blood. Van Holde (1996) teaches one of the roles of insulin is to promote the uptake of fuel

substances into some cells, such as increased uptake of glucose out of the blood and into muscle and adipose tissue and also activation of glycolysis in the liver. Van Holde (1996) at page 826-827 further teaches the relationship between blood glucose levels and insulin levels, such as if you increase insulin levels then blood glucose levels decrease and vice versa under normal circumstance. Van Holde (1996) clearly teaches under normal circumstances that insulin and glucose have an indirect mathematical relationship.

Van Holde (1996) does not explicitly teach calculating the level of blood glucose according to the equation as is instantly claimed.

It would have been obvious to one of ordinary skill in the art to mathematically represent the calculation of a fasting blood glucose level as being indirectly proportionate to the level of insulin as Van Holde (1996) has clearly described in the recited pages. It has been well known by those of ordinary skill in the art that under normal circumstances, if one increases the level of insulin in the blood that its effect is to decrease the glucose level in the blood. It is common to those of ordinary skill in the art to represent such relationships generically and mathematically as an indirect relationship. Furthermore, under normal circumstances insulin will work as predicted and therefore its efficiency will not be altered. Therefore, to represent efficiency as a value of 1, under normal circumstances, would have been obvious to one of ordinary skill in the art and the results would have been unobvious and predictable.

Van Holde (1996) does not explicitly teach having the efficiency value for insulin in the presence of diabetes somewhere between 0-1.

Van Holde (1996) at page 829 teaches that there may be several reasons for the cause of diabetes, such as a mutation in the insulin structure or mutations in the insulin receptors or molecules involved in the conversion of molecules into insulin all of which effect the efficiency of role of insulin. Therefore, to represent the efficiency of insulin under said conditions, it would have been obvious to one of ordinary skill in the art to represent the efficiency of insulin as somewhere between 0-1 depending on the condition and cause and the results would have been unobvious and predictable.

Van Holde (1996) does not specifically teach saving at least one value to a computer storage device.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to store a calculated value to a computer storage device because it is the common practice of those in the field to use computers to perform such calculations and saving a result is common practice to those in the field and would not have produced any unobvious or unpredictable results by doing so.

Response to Arguments:

Applicant's arguments filed 6/10/2008 have been fully considered but they are not persuasive.

Applicant argues that Van Holde (1996) does not teach limitations for “Fasting Plasma Glucose,” which relate to a more specific characterization than simply “glucose level in the blood.”

Applicant's arguments are not found persuasive as Van Holde (1996) at page 826, under Responses to metabolic stress, second paragraph describe the relationship between glucose levels and insulin after a meal, i.e. "Fasting Plasma Glucose," which also describes effects on the production of glucose, i.e. basal hepatic production. Furthermore, Van Holde (1996), page 828-829 also describes the relationship between glucose levels and insulin under other conditions such as diabetes, wherein insulin may be defective and as a result glucose is actually present in excessive amounts. In addition, applicant has not defined or limited that term "fasting plasma glucose" in the instant specification and therefore, glucose levels in the blood after a meal, read on the definition of a "fasting plasma glucose" value.

Applicant further argues that inherency was improperly relied upon in support of the rejection.

Applicant's arguments are not found persuasive they do not point out what exact limitation inherency was relied upon in support of the instant rejection. Therefore, it is unclear as to what exactly applicant's are arguing with respect to stating inherency was improperly relied upon.

Applicant further argues that representing relationships generically and mathematically provides no reasonable expectation of success for the modification proposed with respect to this rejection.

Applicant's arguments are not found persuasive because applicants argue that the mathematical arrangement which describes a relationship between events is unobvious and unpredictable from that of a verbal description about the same

relationship between events. For example, Van Holde (1996) describes the relationship between insulin and glucose levels as such that if you increase insulin levels then blood glucose levels decrease and vice versa under normal circumstance. Therefore, the verbal description of the relationship is teaching that there is an inverse relationship between the two levels, which in mathematics is represented through an inverse function as described. Furthermore, Van Holde (1996) describes how insulin functionality may be effected by events such as mutations, which would cause insulin to not work with 100% efficiency. Therefore, the verbal description is teaching that the insulin value may be altered by a factor between 0-100% in the event such as a mutation, wherein mathematics this effect is often represented through the use of a weighting parameter. Therefore there is nothing found unpredictable about the mathematical relationship claimed and the verbal description provided by Van Holde (1996).

Applicant further argues that the office action does not point out any quatitative characterization of efficiency or even any specific discussion of efficiency in the cited reference.

Applicant's arguments are not found persuasive because in the office action it was stated that Van Holde (1996) at page 829 teaches that there may be several reasons for the cause of diabetes, such as a mutation in the insulin structure or mutations in the insulin receptors or molecules involved in the conversion of molecules into insulin all of which effect the efficiency of role of insulin. Therefore, to represent the efficiency of insulin under said conditions, it would have been obvious to one of

ordinary skill in the art to represent the efficiency of insulin as somewhere between 0-1 depending on the condition and cause and the results would have been unobvious and predictable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jason Sims, whose telephone number is (571)-272-7540.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Marjorie Moran can be reached via telephone (571)-272-0720.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices

published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

// Jason Sims //

/Michael Borin, Ph.D./

Primary Examiner, Art Unit 1631